

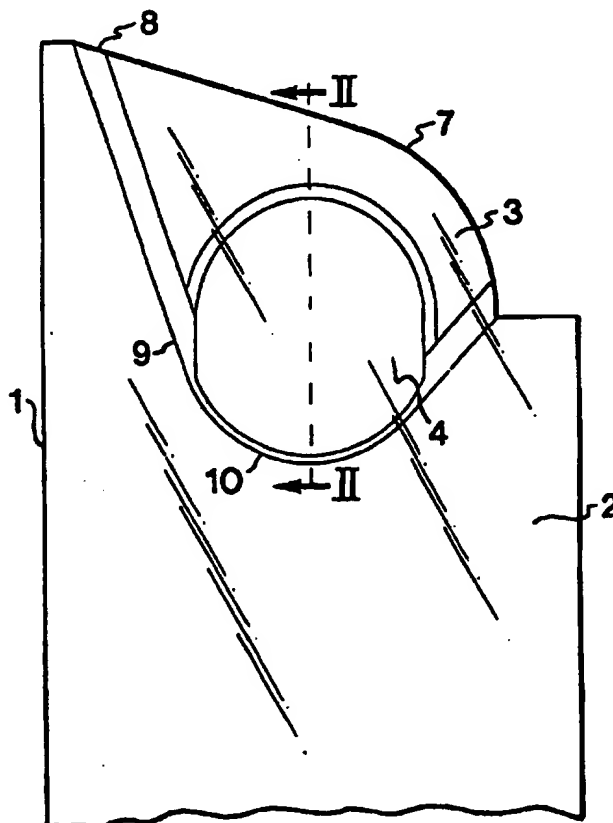


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(21) International Application Number: PCT/SE96/00504 (22) International Filing Date: 18 April 1996 (18.04.96) (30) Priority Data: 9501460-1 21 April 1995 (21.04.95) SE (71) Applicant (for all designated States except US): HEMOCUE AB [SE/SE]; P.O. Box 1204, S-262 23 Ängelholm (SE). (72) Inventors; and (75) Inventors/Applicants (for US only): WILLIAMSSON, Anders [SE/SE]; Konsulns väg 20, S-252 84 Helsingborg (SE). WAHLQVIST, Stefan [SE/SE]; Lingogatan 5, S-234 43 Lomma (SE). NILSSON, Sven-Erik [SE/SE]; Döbeliusgatan 39, S-256 54 Helsingborg (SE). LILJA, Jan [SE/SE]; Södra Brunnsvägen 63, S-253 60 Helsingborg (SE). JANSSON, Lars [SE/SE]; Råggatan 2, S-262 53 Ängelholm (SE). NILSSON, Bertil [SE/SE]; Storkvägen 10, S-237 37 Bjärred (SE). (74) Agent: AWAPATENT AB; P.O. Box 5117, S-200 71 Malmö (SE).		(81) Designated States: AL, AM, AT, AT (Utility model), AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, CZ (Utility model), DE, DE (Utility model), DK, DK (Utility model), EE, EE (Utility model), ES, FI, FI (Utility model), GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK (Utility model), TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>

(54) Title: CAPILLARY MICROCUVETTE**(57) Abstract**

The present invention is related to an integral capillary microcuvette comprising a body member and a cavity including a measuring zone within the body member. The cavity is defined by two opposite, substantially parallel inner surfaces of the body member and includes an outer peripheral edge comprising a sample inlet and an inner peripheral zone having a channel of higher capillary force than the measuring zone. The channel extends around the entire inner peripheral zone with ends of the channel communicating with the atmosphere at the exterior of the microcuvette.



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CAPILLARY MICROCUVETTEBackground of the Invention

The present invention concerns a capillary micro-cuvette. More specifically the invention concerns a disposable integral capillary microcuvette having improved flow for essentially simultaneously sampling a fluid and analyzing of the sample.

A cuvette for sampling a fluid, mixing the sample with a reagent and directly making optical analysis of the sample mixed with the reagent is previously known from US patent 4,088,448. This cuvette comprises a body member including two planar surfaces defining an optical path and placed at a predetermined distance from one another to determine the optical path length and to define a cavity which includes a measuring zone therein, having an inlet for communicating said cavity with the exterior of the body member. The cavity has a predetermined fixed volume, and the predetermined distance permits the sample to enter the cavity by capillary force. Furthermore, a reagent is coated on the cavity surface, which mixes with the sample and allows the sample to be measured by optical analysis.

This known cuvette has several advantages when compared with the conventionally used devices. It permits sampling of a liquid, mixing and chemically reacting it with a suitable reagent; e.g. for colour development, in the same vessel as the one used for the subsequent measurement. The cuvette disclosed in US patent 4,088,448 thus simplifies the sampling procedure, reduces the number of devices needed and in most cases, depending on the type of analysis, considerably improves the accuracy of the analysis by making the analyzing procedure independent of the operation of the device.

However, it has been discovered that the micro-cuvette described in US patent 4,088,488 may develop air bubbles that can interfere with the optical analysis.

**CONFIRMATION
COPY**

Air bubbles generally form in the cavity of the cuvettes because of unsatisfactory sample flow in the cuvette cavity. This is especially detrimental for hemoglobin measurements because of the strong absorption of the hemoglobin. In particular, in a photometric determination, the presence of a large air bubble in the light path traversing the measuring zone will result in an overall measured hemoglobin value below the actual level because the photometer will read the bubble as a contribution of extremely low hemoglobin. Quality control is routinely carried out to discard those cuvettes which include air bubbles, thereby eliminating the risk that air bubbles will be present in the measuring zone when the cuvettes are used in a clinical procedure. A considerable number of cuvettes do not pass the quality control and have to be discarded, thereby increasing the overall cost of the cuvettes.

Object of the Invention

One object of the present invention is to provide an improved cuvette which eliminates the risk of failure caused by the presence of air bubbles in the measuring zone.

Summary of the Invention

The above objects and others are accomplished by providing a disposable, integral capillary microcuvette for essentially simultaneous sampling a fluid and analyzing the sample. In connection with the present invention the term "integral" means that the cuvette is made or manufactured in one, integral, piece. The microcuvette comprises a body member and a cavity including a measuring zone within the body member. The cavity is defined by two opposite, substantially parallel inner surfaces of the body member and includes an outer peripheral edge comprising a sample inlet and an inner

peripheral zone having a channel of higher capillary force than the measuring zone. The channel extends around the entire inner peripheral zone with ends of the channel communicating with the exterior of the micro-
5 cuvette.

Brief Description of the Drawings

Fig 1 is a plan view of the microcuvette according to one embodiment of the present invention.

10 Fig 2 is a cross sectional view of a microcuvette according to the present invention, taken along line II-II of Fig 1.

Fig 3 is a perspective view of the microcuvette according to the invention.

15

Detailed Description of the Invention

Fig 1 is a plan view of a microcuvette generally designated by reference numeral 1, according to one embodiment of the present invention. The microcuvette 1,
20 comprises a body member 2, comprised of two substantially planar sheets of material 11, 12, and includes a cavity 3, defined by two inner surfaces 5, 6, of the body member 2. A measuring zone 4 is arranged within the cavity 3. The distance between the surfaces 5, 6, defining the measuring zone 4, is a critical parameter in
25 providing the proper optical path length for the desired measurement. In a preferred embodiment of measuring hemoglobin, the distance should be between 0.05 and 0.15 mm. The distance between the inner surfaces of the rest of the cavity 3 is preferably in the order of 0.3-2 mm,
30 i.e. clearly longer than the distance between the inner surfaces 5, 6 of the measuring zone. An outer peripheral edge 7, includes a sample inlet 8, comprised of the opening between the two sheets 11, 12, making up the
35 body member 2. An inner peripheral zone 9, includes a channel 10, which has a higher capillary force than the

measuring zone 4. The channel 10, which can have any shape, extends along the entire inner peripheral zone 9, and communicates with the atmosphere at both ends of the channel 10. The channel 10, preferably has a width between 10 micron and 2 mm.

When a sample liquid is drawn into the cuvette through the inlet 8, the channel 10 is filled along its entire length due to its high capillary action. After the filling of the channel the sample liquid propagates into the rest of the cavity 3 in a flow pattern which prevents air bubbles to be captured in the measuring zone 4.

The provision of the channel having a higher capillary force than the measuring zone thus improves hydrodynamic flow within the cuvette cavity and prevents air bubbles to be trapped in the measuring zone. The channel may have any appropriate shape or form as long as the capillary force of the channel is higher than the capillary force of the measuring zone. This is accomplished by providing a channel having a depth which is less than that of the measuring zone. In particular, the channel may be defined by an inner wall of the inner peripheral zone and by the two opposite, substantially planar, surfaces of the body member whereby the distance between the planar surfaces of the channel is shorter than the distance between the inner surfaces of the measuring zone.

In an alternative embodiment of the present invention, the distance between the two opposite substantially planar surfaces of the body member continuously increases in a direction extending away from the inner end wall of the inner peripheral zone. In this case the channel is shaped as a wedge, the bottom of which opens towards the measuring zone.

The cuvettes according to the present invention may be formed from any suitable material which allows the

formation of the channel and measuring zone to the necessary tight tolerance levels. Preferably, the cuvettes according to the present invention are made of glass or a polymeric material.

5 Cuvettes according to the present invention were compared with cuvettes according to US patent 4,088,488 as follows:

A reagent of

 40g sodium desoxycholate
10 18g sodium azid and
 20g sodium nitrite

per liter solvent was prepared.

 100 cuvettes according to US patent 4,088,488 available from HemoCue AB, Sweden, and 100 cuvettes according to the present invention were filled with the
15 above reagent, air dried and examined optically for uniform drying pattern. The cuvettes were then filled with whole blood, EDTA and an anticoagulating agent. A hemoglobin measurement was then carried out according to a
20 modified azidmethemoglobin method according to Vanzetti described in J. Lab. Clin. Med. 67, 116-26 (1966) measuring at 570 nm and 880 nm respectively. The number of cuvettes which exhibited air bubbles was recorded.

25	Type of Cuvette	Number with air bubble
	US 4,088,488	25
	The invention	0

 As is apparent from the above, the cuvettes according to the present invention are very advantageous in
30 eliminating the risks associated with the occurrence of air bubbles within the measuring zone. By providing the cuvette according to the present invention with a channel having higher capillary force than that of the measuring zone, air bubbles were entirely eliminated. This
35 not only reduced the costs associated with discarded cu-

vettes but also greatly reduces the risk of improper readings which occur because of air bubbles.

The present invention has been described above with respect to the measurement of hemoglobin. However, the
5 present invention is equally applicable to the measurement of other blood chemistry values, such as glucose, blood urea nitrogen, albumin, bilirubin, and total protein, etc. Furthermore, the present invention is applicable to numerous other analytical measurements and
10 tests outside the blood chemistry field.

The foregoing has been a description of certain preferred embodiments of the present invention, but it is not intended to limit the invention in any way. Rather, many modifications, variations, and changes in
15 details may be made within the scope of the present invention.

WHAT IS CLAIMED

1. An integral capillary microcuvette (1) comprising a body member (2) and a cavity (3) including a measuring zone (4) within the body member (2), the cavity (3) being defined by two opposite, substantially parallel inner surfaces (5,6) of the body member, an outer peripheral edge (7) including a sample inlet (8) and an inner peripheral zone (9) having a channel (10) of higher capillary force than the measuring zone (4), both ends of the channel (10) communicating with the exterior of the microcuvette (1).

2. A microcuvette according to claim 1, wherein said channel (10) is defined by an inner end wall of said inner peripheral zone (9) and two substantially planar surfaces of said body member.

3. A microcuvette (1) according to claim 2, wherein said two substantially planar surfaces are parallel and the distance therebetween is less than the distance between the inner surfaces (5,6) defining said measuring zone (4).

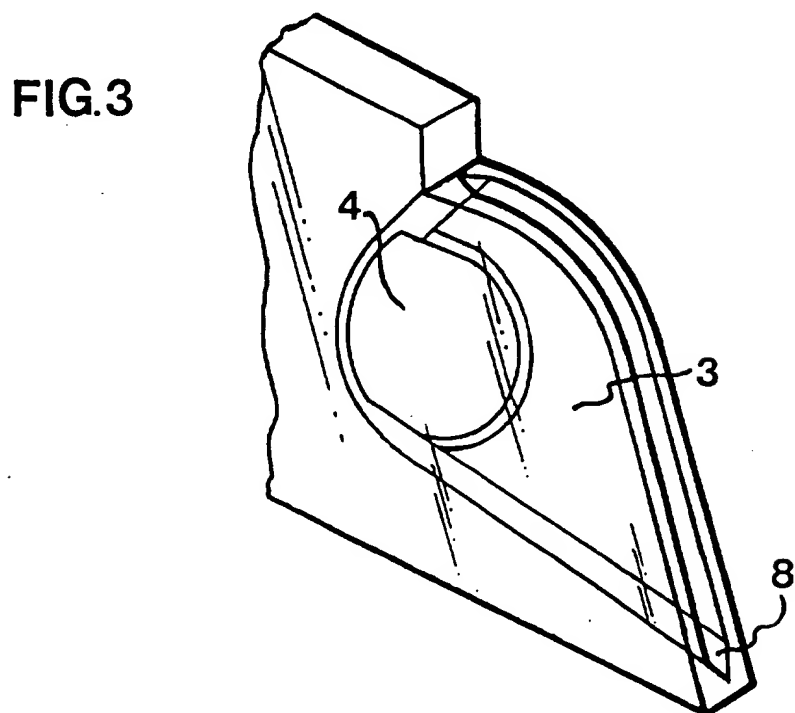
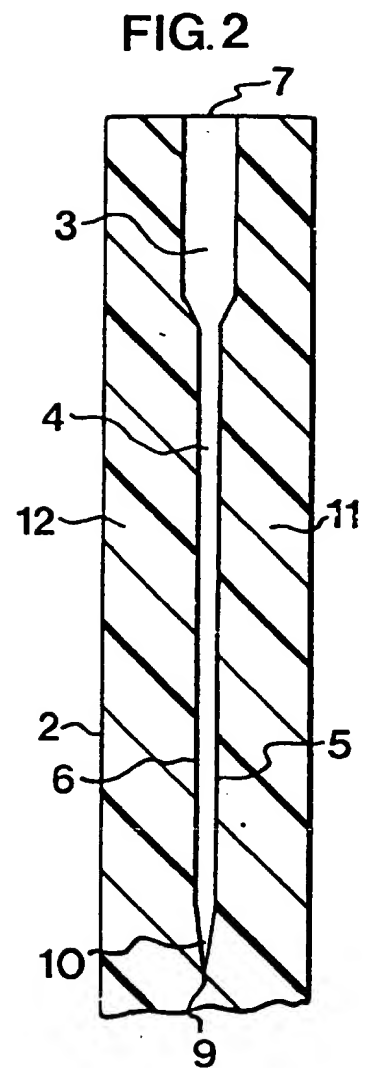
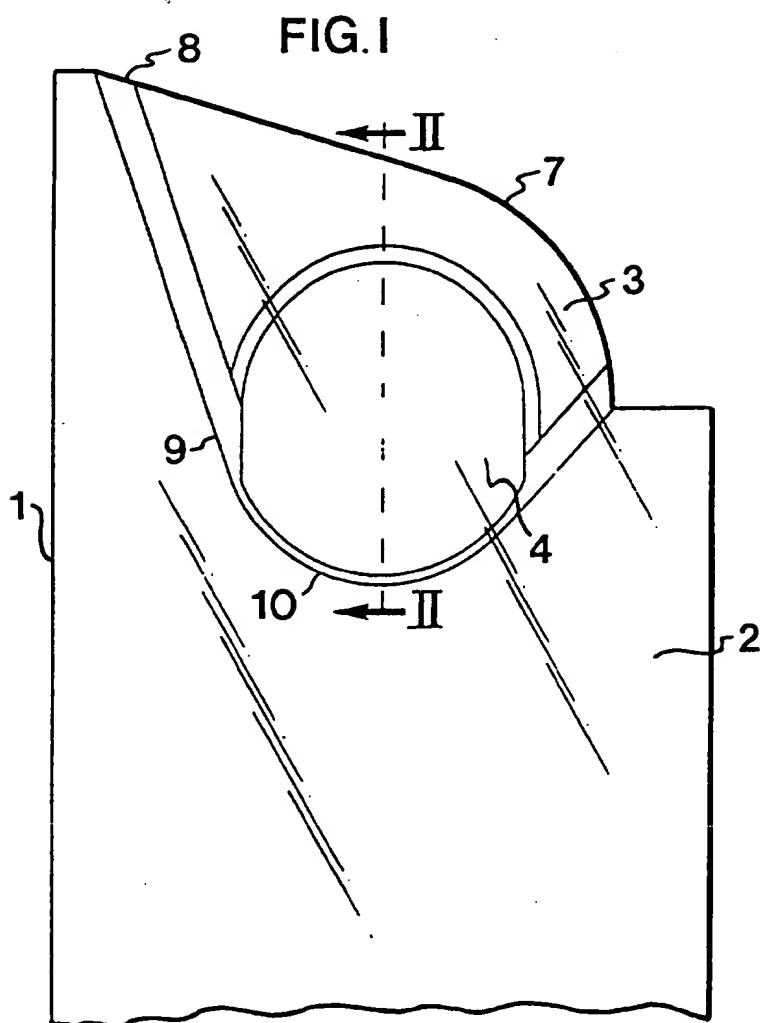
4. A microcuvette (1) according to claim 2, wherein the distance between the two substantially planar surfaces of said body member (2) increases in a direction extending away from said inner end wall of said inner peripheral zone (9).

5. A microcuvette (1) according to claim 1, wherein said cavity (3) has predetermined volume.

6. A microcuvette (1) according to claim 1, wherein said cavity (3) includes a dry reagent in a predetermined amount.

7. A microcuvette (1) according to claim 1, for use in the determination of hemoglobin in undiluted whole blood, wherein said measuring zone has depth that does not exceed 0.15 mm.

8. A microcuvette (1) according to claim 7, wherein hemoglobin is determined by the azidmethemoglobin method.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 96/00504

A. CLASSIFICATION OF SUBJECT MATTER

IPC6: G01N 21/03, B01L 3/80

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC6: G01N, B01L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPODOC, WPI

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0287883 A ¹ (MILES INC.), 26 October 1988 (26.10.88), figure 2, abstract --	1-8
A	US 3705000 A (J.P. GUERRA), 5 December 1972 (05.12.72), column 2, line 15 - line 62, figures 1, 2 --	1-8
A	Patent Abstracts of Japan, Vol 14, No 160, P-1028, abstract of JP, A, 2-17426 (KIYOUSEKI SEIHIN GIJUTSU KENKYUSHO K.K.), 22 January 1990 (22.01.90) -- -----	1-8

☐ Further documents are listed in the continuation of Box C.☒ See patent family annex.

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INTERNATIONAL SEARCH REPORT
Information on patent family members

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A1- 0287883	26/10/88	AU-A- 1452788 CA-A- 1315181 JP-A- 63274839	13/10/88 30/03/93 11/11/88
US-A- 3705000	05/12/72	CA-A- 938126	11/12/73